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EXAMINER

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/735,395	<b>Applicant(s)</b> GRUBER ET AL.	
	<b>Examiner</b> STEPHANIE K. MUMMERT	<b>Art Unit</b> 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 22 April 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,13,18,57,61,87,88,103,112,130,149 and 158-206 is/are pending in the application.
- 4a) Of the above claim(s) 103,130 and 149 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,13,18,57,61,87,88,112 and 158-206 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 22, 2008 has been entered.

Applicant's amendment filed on April 22, 2008 is acknowledged and has been entered. Claims 1, 13, 18, 57 and 87-88 have been amended. Claims 2-12, 14-17, 19-56, 58-60, 62-86, 89-102, 104-111, 113-129, 131-148, 150-157 have been canceled. Claims 158-206 have been added. Claims 1, 13, 18, 57, 61, 87-88, 112 and 158-206 are pending. Claims 103, 130 and 149 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 1, 13, 18, 57, 61-62, 87-88, 112 and 158-206 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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**This action is made NON-FINAL to address newly added claims and claims previously indicated allowable.**

***Allowable Subject Matter***

The indicated allowability of claims 57 and 61 is withdrawn in view of the newly discovered reference(s) to Grier. Rejections based on the newly cited reference(s) follow.

***New Grounds of Rejection necessitated by amendment***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 187-189, 191, 193-197, 200-202 recite the limitation "the phase patterning element" in the body of the claim. These claims depend from either claim 57 or claim 88, and neither of these claims recite the term "the phase patterning element". There is insufficient antecedent basis for this limitation in the claim.

***New Grounds of Rejection made below over newly cited claims and over claims previously indicated as allowable***

***Claim Interpretation***

The term "wherein the probes which react with the targets are segregated from the remaining probes" is not explicitly defined in the specification. Therefore, the term is being

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broadly interpreted as reading on the claimed optional lack of interaction with the target and therefore no segregation is performed. In this case a 102 over Grier (6,416,190) will be applied.

In a more narrow interpretation where targets are reacted and interact, segregation, by movement is viewed as obvious in view of the independent movement taught by Grier (6,055,106). In this case, a 103 over Grier in view of Ulmer and Visscher will be applied.

***New Grounds of Rejection over new claims***

***Claim Rejections - 35 USC § 103***

1. Claims 177-180, 182-183 and 185-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grier II (US Patent 6,416,190; July 2002) as applied to claims 1, 13, 18, 57, 61, 87-88, 112, 159, 162-164, 166, 170, 175-176, 181, 184, 187-189 and 191-206 above, and further in view of Shivashankar et al. (US Patent 6,139,831; October 2000). Grier II teaches an apparatus and method for manipulating particles using optical traps (Abstract).

Grier teaches all of the limitations of claims 1, 13, 18, 57, 61, 87-88, 112, 159, 162-164, 166, 170, 175-176, 181, 184, 187-189 and 191-206 as recited above. Grier does not teach that the probes are bound to a substrate. Shivashankar teaches the use of optical traps in connection to substrate arrays (Abstract).

With regard to claim 177, Shivashankar teaches an embodiment of claim 176, wherein at least one of the probes is one of bound to a substrate or unbound to a substrate (Figure 5B, where particles trapped in an optical tweezer are grafted onto a substrate).

With regard to claim 178, Shivashankar teaches an embodiment of claim 177, wherein all the substrate bound probes having the same binding or reactivity characteristic are labeled with

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the same markers (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 179, Shivashankar teaches an embodiment of claim 178, wherein at least one of the markers is a wavelength specific dye (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 180, Shivashankar teaches an embodiment of claim 179, wherein at least one of the substrate bound probes is selected by measuring the spectral response of the wavelength specific dye and using the spectral measurement to select the at least one probe (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C)

With regard to claim 182, Shivashankar teaches an embodiment of claim 177, wherein at least one of the probes is bound to a substrate labeled with a wavelength specific marker and the at least one bound probe is selected by spectroscopically measuring the marker and using the spectroscopic measurement to select the at least one probe (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 183 and 186, Shivashankar teaches an embodiment of claim 57, further comprising moving at least one of the trapped probes by transferring the probe from one optical trap to another (coll. 18, lines 9-30).

With regard to claim 185, Shivashankar teaches an embodiment of claim 57, wherein at least some probes are bound to a substrate and at least some probes are unbound to substrate (Figure 5B, wher particles trapped in an optical tweezer are grafted onto a substrate).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Grier to include the physical substrate of Shivashankar to arrive at the claimed invention with a reasonable expectation for success. As taught by Shivashankar, “by using an optical tweezer as a non-invasive tool, a particle coated with a molecule, such as a biomolecule, can be selected and grafted onto spatially localized positions of a semiconductor substrate” (col. 18, lines 31-41). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Grier to include the physical substrate of Shivashankar to arrive at the claimed invention with a reasonable expectation for success.

2. Claims 177-180, 182-183 and 185-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grier I (US Patent 6,055,106; April 2000) in view of Ulmer et al. (US Patent 5,776,674; July 1998) and further in view of Visscher et al. (IEEE Journal of Selected Topics in Quantum Electronics, 1996, vol. 2, p. 1066-1076) as applied to claims 1, 13, 18, 57, 61, 87-88, 112 and 158-176, 181, 184 and 187-206 above and further in view of Shivashankar et al. (US Patent 6,139,831; October 2000). Grier I teaches an apparatus and method for manipulating particles using optical traps (Abstract).

Grier I teaches all of the limitations of claims 1, 13, 18, 57, 61, 87-88, 112 and 158-164, 166-176, 181, 184 and 187-206 as recited above. Grier does not teach that the probes are bound to a substrate. Shivashankar teaches the use of optical traps in connection to substrate arrays (Abstract).

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With regard to claim 177, Shivashankar teaches an embodiment of claim 176, wherein at least one of the probes is one of bound to a substrate or unbound to a substrate (Figure 5B, where particles trapped in an optical tweezer are grafted onto a substrate).

With regard to claim 178, Shivashankar teaches an embodiment of claim 177, wherein all the substrate bound probes having the same binding or reactivity characteristic are labeled with the same markers (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 179, Shivashankar teaches an embodiment of claim 178, wherein at least one of the markers is a wavelength specific dye (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).

With regard to claim 180, Shivashankar teaches an embodiment of claim 179, wherein at least one of the substrate bound probes is selected by measuring the spectral response of the wavelength specific dye and using the spectral measurement to select the at least one probe (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C)

With regard to claim 182, Shivashankar teaches an embodiment of claim 177, wherein at least one of the probes is bound to a substrate labeled with a wavelength specific marker and the at least one bound probe is selected by spectroscopically measuring the marker and using the spectroscopic measurement to select the at least one probe (col. 17, lines 58-63, where the probes are labeled with a wavelength specific marker; see also Figure 4C).



With regard to claim 183 and 186, Shivashankar teaches an embodiment of claim 57, further comprising moving at least one of the trapped probes by transferring the probe from one optical trap to another (coll. 18, lines 9-30).

With regard to claim 185, Shivashankar teaches an embodiment of claim 57, wherein at least some probes are bound to a substrate and at least some probes are unbound to substrate (Figure 5B, where particles trapped in an optical tweezer are grafted onto a substrate).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Grier to include the physical substrate of Shivashankar to arrive at the claimed invention with a reasonable expectation for success. As taught by Shivashankar, “by using an optical tweezer as a non-invasive tool, a particle coated with a molecule, such as a biomolecule, can be selected and grafted onto spatially localized positions of a semiconductor substrate” (col. 18, lines 31-41). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Grier to include the physical substrate of Shivashankar to arrive at the claimed invention with a reasonable expectation for success.

***New Grounds of rejection***

***Previous Rejections Adjusted to address claims 57, 61 and new claims 199-206***

***Claim Rejections - 35 USC § 102***

3. Claims 1, 13, 18, 57, 61, 87-88, 112, 159, 162-164, 166, 170, 175-176, 181, 184, 187-189 and 191-206 are rejected under 35 U.S.C. 102(e) as being anticipated by Grier II (US Patent

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6,416,190; July 2002). Grier II teaches an apparatus and method for manipulating particles using optical traps (Abstract).

With regard to claim 1, Grier teaches a method of configuring and tracking an array of probes comprising:

- a) generating at least two independently movable optical traps within a vessel (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);
- b) providing at least two probes within the vessel (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array);
- c) selecting at least two of the probes for inclusion in an array of probes contained within the optical traps based on predetermined binding and reactivity characteristics of the probes (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);
- d) trapping each of the selected probes having said predetermined binding and reactivity characteristics with a corresponding one of the optical traps to configure the array of probes contained within the optical traps (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics); and,

e) tracking the position of at least one of the trapped probes in the array by computerized monitoring of the position of the optical trap which contains it (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles through monitoring of their position).

With regard to claim 13, Grier teaches an embodiment of claim 1, wherein the trapped probe is a chemical compound or biological material (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological).

With regard to claim 18, Grier teaches an embodiment of claim 1 wherein the trapped probe is at least one of an oligonucleotide, a polynucleotide, a protein, a polysaccharide, a ligand, a cell, an antibody, an antigen, a cellular organelle, a lipid, a blastomere, an aggregations of cells, a microorganism, a peptide, cDNA, RNA or combinations thereof (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle).

With regard to claim 57, Grier teaches a method of assaying biological material comprising:

- a) generating at least two independently movable optical traps within a vessel (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);
- b) providing a fluid media in the vessel; providing at least two probes for biological materials within the fluid media (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in

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the array);

c) selecting at least two of the probes for inclusion in an array based on predetermined binding and reactivity characteristics of the probes (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);

d) trapping each of the selected probes having said predetermined binding and reactivity characteristics with a corresponding one of the optical traps (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);

introducing into the vessel at least one target comprised of a biological material (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle; Examples 1-3, where a variety of cells were analyzed); and, determining the reaction or lack thereof, of each of the trapped probes with each of the targets; wherein the probes which react with the targets are segregated from the remaining probes (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle; Examples 1-3, where a variety of cells were analyzed).

With regard to claim 61, Grier teaches an embodiment of claim 57, wherein the trapped probe is at least one of an oligonucleotide, a polynucleotide, a protein, a polysaccharide, a ligand,

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a cell, an antibody, an antigen, a cellular organelle, a lipid, a blastomere, an aggregations of cells, a microorganism, a peptide, cDNA, RNA at combinations thereof (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle).

With regard to claim 87, Grier teaches a method of configuring an array of probes comprising:

- a) generating at least two independently movable optical traps within a vessel (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);
  - b) providing at least two probes within the vessel (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array); and,
  - c) configuring an array of at least two probes by selecting each probe with a corresponding one of the optical traps based on predetermined binding and reactivity characteristics of the probes (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);
- wherein said array is modifiable by removing or adding at least one probe in said array (col. 7, lines 44-50, where the optical traps can be used to 'remove or add particles at various optical trap sites').

With regard to claim 88, Grier teaches a method of configuring and reconfiguring an array of probes comprising:

- a) directing a focused beam of light at a phase patterning optical element to form a plurality of beamlets emanating from the phase patterning optical element (col. 4, lines 52-65);
- b) directing the plurality of beamlets at the back aperture of a focusing lens to pass the beamlets through the focusing lens and converge the beamlets emanating from the focusing lens to generate independently movable optical traps within a vessel (col. 5, lines 22-30, where a focusing optical element converges the beams);
- c) providing a plurality of probes within the vessel (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are a plurality of probes or particles trapped in the array);
- d) selecting at least two of the probes for inclusion in the array of probes contained within the optical traps based on predetermined binding and reactivity characteristics of the probes (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics);
- e) trapping each of the selected probes with said predetermined binding and reactivity characteristics with a corresponding one of the optical traps to configure the array of probes contained within the optical traps (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles; where the

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biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics); and,

f) altering the position of at least one of the probes contained within the array by moving the optical trap containing the probe to reconfigure the array of probes contained within the optical traps (col. 7, lines 44-60, where the optical traps can be moved).

With regard to claim 112, Grier teaches an embodiment of claim 1, wherein the movement of the trapped probes are tracked based on pre-determined movement of each optical trap caused by encoding the phase patterning optical element (col. 7, line 63 to col. 8, line 12, where the hologram is computer designed and provides a pattern of phase modulations).

With regard to claim 159, Grier teaches an embodiment of claim 57, wherein the trapped probe is comprised of one of a biological material or a chemical compound (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle; Examples 1-3, where a variety of cells were analyzed).

With regard to claim 162, Grier teaches an embodiment of claim 57, wherein each optical trap is movable independently (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 163, Grier teaches an embodiment of claim 57, wherein the movement of each optical trap is controlled by a computer (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram, which is controlled by a computer).

With regard to claim 166 and 170, Grier teaches an embodiment of claim 165 and 169, further comprising using the computer to direct the movement of one or more optical traps based on the analysis of the optical data stream (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram, which is controlled by a computer).

With regard to claim 175 and 206, Grier teaches an embodiment of claim 57, wherein the optical traps are formed of two or more of optical tweezers, optical vortices, optical bottles, optical rotators, and light cages (col. 8, lines 11-12, where the optical traps are optical tweezers).

With regard to claim 176, Grier teaches an embodiment of claim 57, wherein at least two of the probes have binding or reactivity characteristics that differ from one another and at least one of the probes is selected by segregating the probe based on its different binding or reactivity characteristic by moving the probe to a predetermined location within the vessel and using the location of the segregated probe to select the probe (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles; where the biomolecules trapped in the optical traps inherently have predetermined binding and reactivity characteristics; and col. 7, lines 44-60, where the optical traps can be moved).

With regard to claim 181, Grier teaches an embodiment of claim 176, wherein the predetermined location is one of a physical sub-cell or an optical sub-cell (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles; where the biomolecules trapped in the optical traps inherently have predetermined



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binding and reactivity characteristics; and col. 7, lines 44-60, where the optical traps can be moved).

With regard to claim 184, Grier teaches an embodiment of claim 57, wherein the probes are all directly trapped by the optical trap (col. 8, lines 11-12, where the optical traps are optical tweezers and where these probes or particles are directly trapped).

With regard to claim 187 and 194, Grier teaches an embodiment of claim 57 and 193, wherein the phase patterning optical element has a static surface having two or more discrete regions and the position of at least one optical trap is altered by changing the discrete region of the static surface to which the beam of light is directed (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 188 and 201, Grier teaches an embodiment of claim 57 and 200, wherein the phase patterning optical element is dynamic and varying the phase patterning optical element alters the position of the at least one optical trap (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 189, Grier teaches an embodiment of claim 57, wherein the phase patterning optical element is dynamic and varying the phase patterning optical element changes the form of at least one of the optical traps to an optical tweezer, an optical vortex, an optical bottle, an optical rotator, or a light cage (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 191, Grier teaches an embodiment of claim 158, further comprising moving the optical trap containing the tracked probe by changing the surface of the phase

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patterning optical element (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 192 and 205, Grier teaches an embodiment of claim 88 or 176, wherein the probes are segregated using movement by optical traps, flow channels or micro-capillaries (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 193, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element has a static surface (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element).

With regard to claim 194, Grier teaches an embodiment of claim 193, wherein the static surface is comprised of two or more discrete regions (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 195, Grier teaches an embodiment of claim 194, wherein the position of at least one of the probes contained within the optical traps is altered by changing the discrete region of the static surface to which the beam of light is directed (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 196, Grier teaches an embodiment of claim 195, wherein the static surface is substantially continuously varying (Figure 5, where continuous translation of the optical traps are possible; see col. 5, lines 61-67).

With regard to claim 197, Grier teaches an embodiment of claim 194, wherein the position of the at least one optical trap is altered by changing the region of the static surface to which the beam of light is directed (col. 4, lines 52-65; col. 5, lines 1-11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 198, Grier teaches an embodiment of claim 88, wherein the beam altering optical element is a grating, a hologram, a stencil, a light shaping holographic filter, a lens, a mirror, a prism, or a waveplate (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 199, Grier teaches an embodiment of claim 194, wherein each discrete region is a grating, a hologram, a stencil, a light shaping holographic filter, a lens, a mirror, a prism, or a waveplate (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 200, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element is dynamic (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram and where this can be dynamically altered).

With regard to claim 202, Grier teaches an embodiment of claim 200, wherein the form of at least one of the optical traps is changed by varying the dynamic phase patterning optical element (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

With regard to claim 203, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element has a discrete static surface, and wherein a form of at least one of the optical traps is changed by moving the discrete static surface (col. 4, lines 52-65; col. 5, lines 1-

11, where the light arrives at an optical diffractive element and where different points of diffraction are possible).

With regard to claim 204, Grier teaches an embodiment of claim 202, wherein the varying of the dynamic phase patterning optical element is a change in a hologram encoded on its surface (col. 7, line 63 to col. 8, line 12, where one of the beam altering optical elements is a phase only hologram).

***Claim Rejections - 35 USC § 103***

4. Claims 1, 13-18, 57, 61, 87-88, 112 and 158-176, 181, 184 and 187-206 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grier I (US Patent 6,055,106; April 2000) in view of Ulmer et al. (US Patent 5,776,674; July 1998) and further in view of Visscher et al. (IEEE Journal of Selected Topics in Quantum Electronics, 1996, vol. 2, p. 1066-1076). Grier teaches an apparatus and method for manipulating particles using optical traps (Abstract).

With regard to claim 1, Grier teaches a method of configuring and tracking an array of probes comprising:

- a) generating at least two independently movable optical traps within a vessel (col. 2, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 5, lines 12-18, where it is noted that the optical tweezer system can be used to actively move particles relative to one another);
- b) providing at least two probes within the vessel (col. 2, lines 9-18, where the method is directed to trapping small dielectric particles or other materials, and col. 2, lines 48-57, where it is noted that an object of the invention includes chemical and biosensor arrays, facilitation of combinatorial chemistry applications and manipulation of biological materials);

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c) selecting at least two of the probes for inclusion in an array of probes contained within the optical traps (col. 2, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 2, lines 62-66, where the method is directed to the construction of a spatial array of optical traps for manipulation of particles);

d) trapping each of the selected probes with a corresponding one of the optical traps to configure the array of probes contained within the optical traps (col. 4, lines 29-30 and lines 58-65, where embodiments of arbitrary arrays of trapped particles are described; Figure 7, where a 4x4 array of beams is used to trap sixteen silica spheres in sixteen optical tweezers); and,

e) tracking at least one of the trapped probes in the array by computerized monitoring of the optical trap which contains it (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles).

With regard to claim 13, Grier teaches an embodiment of claim 1, wherein the trapped probe is one of a chemical compound or a biological material (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological).

With regard to claim 18, Grier teaches an embodiment of claim 1 wherein the trapped probe is an oligonucleotide, a polynucleotide, a protein, a polysaccharide, a ligand, a cell, an antibody, an antigen, a cellular organelle, a lipid, a blastomere, an aggregations of cells, a microorganism, a peptide, cDNA, RNA or combinations thereof (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological; col. 12, lines 31-34, where an example of a trapped biological is a chloroplast which comprises a cellular organelle).

With regard to claim 57, Grier teaches a method of assaying biological material comprising:

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- a) generating at least two independently movable optical traps within a vessel (col. 2, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 5, lines 12-18, where it is noted that the optical tweezer system can be used to actively move particles relative to one another);
- b) providing a fluid media in the vessel; providing at least two probes for biological materials within the fluid media (col. 2, lines 9-18, where the method is directed to trapping small dielectric particles or other materials, and col. 2, lines 48-57, where it is noted that an object of the invention includes chemical and biosensor arrays, facilitation of combinatorial chemistry applications and manipulation of biological materials);
- c) selecting at least two of the probes for inclusion in an array based on predetermined binding and reactivity characteristics of the probes (col. 2, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 2, lines 62-66, where the method is directed to the construction of a spatial array of optical traps for manipulation of particles);
- d) trapping each of the selected probes having said predetermined binding and reactivity characteristics with a corresponding one of the optical traps (col. 4, lines 29-30 and lines 58-65, where embodiments of arbitrary arrays of trapped particles are described; Figure 7, where a 4x4 array of beams is used to trap sixteen silica spheres in sixteen optical tweezers);
- e) introducing into the vessel at least one target comprised of a biological material (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles).

With regard to claim 61, Grier teaches an embodiment of claim 57, wherein the trapped probe is at least one of an oligonucleotide, a polynucleotide, a protein, a polysaccharide, a ligand, a cell, an antibody, an antigen, a cellular organelle, a lipid, a blastomere, an aggregations of cells,

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a microorganism, a peptide, cDNA, RNA at combinations thereof (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological).

With regard to claim 87, Grier teaches a method of configuring an array of probes comprising:

- a) generating at least two independently movable optical traps within a vessel (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);
  - b) providing at least two probes within the vessel (col. 7, lines 6-20, where the filling of the optical traps with particles, or probes, is described in detail; Figure 9, where there are more than 2 probes or particles trapped in the array); and,
  - c) configuring an array of at least two probes by selecting each probe with a corresponding one of the optical traps (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles);
- wherein said array is modifiable by removing or adding at least one probe in said array (col. 7, lines 44-50, where the optical traps can be used to 'remove or add particles at various optical trap sites');
- d) tracking at least one of the trapped probes in the array by computerized monitoring of the optical trap which contains it (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles).

With regard to claim 88, Grier teaches a method of configuring and reconfiguring an array of probes comprising:

- a) directing a focused beam of light at a phase patterning optical element to form a plurality of beamlets emanating from the phase patterning optical element (col. 4, lines 29-65, specifically lines 29-42, where light passes through a diffractive optical element and a plurality of beams are created);
- b) directing the plurality of beamlets at the back aperture of a focusing lens to pass the beamlets through the focusing lens and converge the beamlets emanating from the focusing lens to generate independently movable optical traps within a vessel (col. 3, lines 36-40, where one or more beams of light are projected into the center of a back aperture; col. 4, line 66 to col. 5, line 7);
- c) providing a plurality of probes within the vessel (col. 1, lines 9-18, where the method is directed to trapping small dielectric particles or other materials, and col. 1, lines 48-57, where it is noted that an object of the invention includes chemical and biosensor arrays, facilitation of combinatorial chemistry applications and manipulation of biological materials);
- d) selecting at least two of the probes for inclusion in the array of probes contained within the optical traps (col. 1, lines 24-47, where the method is directed to the generation of a plurality of optical traps; col. 1, lines 62-66, where the method is directed to the construction of a spatial array of optical traps for manipulation of particles);
- e) trapping each of the selected probes with said predetermined binding and reactivity characteristics with a corresponding one of the optical traps to configure the array of probes contained within the optical traps (col. 4, lines 29-30 and lines 58-65, where embodiments of



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arbitrary arrays of trapped particles are described; Figure 7, where a 4x4 array of beams is used to trap sixteen silica spheres in sixteen optical tweezers); and,

f) altering the position of at least one of the probes contained within the array by moving the optical trap containing the probe to reconfigure the array of probes contained within the optical traps (col. 5, lines 12-18, where it is noted that the optical tweezer system can be used to actively move particles relative to one another);

g) tracking at least one of the trapped probes in the array by computerized monitoring of the optical trap which contains it (col. 7, line 63 to col. 8, line 12, where a personal computer is used to identify specific particles).

With regard to claim 112, Grier teaches an embodiment of claim 1, wherein the movement of the trapped probes are tracked based on pre-determined movement of each optical trap caused by encoding the phase patterning optical element (col. 2, lines 41-45, where an object of the invention is to create multiple independently steered optical traps; col. 5, lines 38-52).

With regard to claim 159, Grier teaches an embodiment of claim 57, wherein the trapped probe is comprised of one of a biological material or a chemical compound (col. 2, lines 44-48, where the material trapped is mechanical, chemical or biological).

With regard to claim 161, Grier teaches an embodiment of claim 57, further comprising altering a position of at least one trapped probe in the array by moving the optical trap containing the probe (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 162, Grier teaches an embodiment of claim 57, wherein each optical trap is movable independently (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 163, Grier teaches an embodiment of claim 57, wherein the movement of each optical trap is controlled by a computer (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram).

With regard to claim 164, Grier teaches an embodiment of claim 160, further comprising receiving the optical data-stream with a computer (Figure 10, where a personal computer is included for imaging of the particles).

With regard to claim 166 and 170, Grier teaches an embodiment of claim 165 and 169, further comprising using the computer to direct the movement of one or more optical traps based on the analysis of the optical data stream (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram).

With regard to claim 175 and 206, Grier teaches an embodiment of claim 57 and 88, wherein the optical traps are formed of two or more of optical tweezers, optical vortices, optical bottles, optical rotators, and light cages (col. 5, lines 12-21, where the optical traps are optical tweezers).

With regard to claim 176, Grier teaches an embodiment of claim 57, wherein at least one of the probes is selected by segregating the probe by moving the probe to a predetermined location within the vessel and using the location of the segregated probe to select the probe (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are

used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 181, Grier teaches an embodiment of claim 176, wherein the predetermined location is one of a physical sub-cell or an optical sub-cell (col. 7, line 6 to col. 8, line 12; see especially col. 8, lines 5-12, where an array of optical traps are used to trap particles that are able to be manipulated individually, indicating the ability to independently move for the particles).

With regard to claim 184, Grier teaches an embodiment of claim 57, wherein the probes are all directly trapped by the optical trap (col. 6, lines 9-12, where the probes are stably trapped in the optical trap).

With regard to claim 187 and 194, Grier teaches an embodiment of claim 57 and 193, wherein the phase patterning optical element has a static surface having two or more discrete regions and the position of at least one optical trap is altered by changing the discrete region of the static surface to which the beam of light is directed (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 188 and 201, Grier teaches an embodiment of claim 57 and 200, wherein the phase patterning optical element is dynamic and varying the phase patterning optical element alters the position of the at least one optical trap (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another).

With regard to claim 189, Grier teaches an embodiment of claim 57, wherein the phase patterning optical element is dynamic and varying the phase patterning optical element changes the form of at least one of the optical traps to an optical tweezer, an optical vortex, an optical

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bottle, an optical rotator, or a light cage (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another).

With regard to claim 191, Grier teaches an embodiment of claim 158, further comprising moving the optical trap containing the tracked probe by changing the surface of the phase patterning optical element (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another).

With regard to claim 192 and 205, Grier teaches an embodiment of claim 88 and 176, wherein the probes are segregated using movement by optical traps, flow channels or micro-capillaries (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another and where this movement can be used to effect segregation).

With regard to claim 193, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element has a static surface (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 195, Grier teaches an embodiment of claim 194, wherein the position of at least one of the probes contained within the optical traps is altered by changing the discrete region of the static surface to which the beam of light is directed (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 196, Grier teaches an embodiment of claim 195, wherein the static surface is substantially continuously varying (col. 5, lines 22-36, where in this embodiment a system is constructed that carries out continuous translation of the optical tweezer trap).

With regard to claim 197, Grier teaches an embodiment of claim 194, wherein the position of the at least one optical trap is altered by changing the region of the static surface to

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which the beam of light is directed (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 198, Grier teaches an embodiment of claim 88, wherein the beam altering optical element is a grating, a hologram, a stencil, a light shaping holographic filter, a lens, a mirror, a prism, or a waveplate (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram).

With regard to claim 199, Grier teaches an embodiment of claim 194, wherein each discrete region is a grating, a hologram, a stencil, a light shaping holographic filter, a lens, a mirror, a prism, or a waveplate (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram).

With regard to claim 200, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element is dynamic (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another and where this movement can be used to effect segregation).

With regard to claim 202, Grier teaches an embodiment of claim 200, wherein the form of at least one of the optical traps is changed by varying the dynamic phase patterning optical element (col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another and where this movement can be used to effect segregation).

With regard to claim 203, Grier teaches an embodiment of claim 88, wherein the phase patterning optical element has a discrete static surface, and wherein a form of at least one of the optical traps is changed by moving the discrete static surface (col. 5, lines 12-21, where the optical trap can have either static or dynamic diffractive optical elements).

With regard to claim 204, Grier teaches an embodiment of claim 202, wherein the varying of the dynamic phase patterning optical element is a change in a hologram encoded on its surface (col. 4, lines 56-65, where the movement of the optical traps can be controlled by a computer generated hologram; col. 5, lines 16-21, where dynamic elements can be used to actively move particles and media relative to one another and where this movement can be used to effect segregation).

Regarding claims 1, 57 and 87-88, Grier does not teach the limitation of selecting probes based on predetermined binding and reactivity characteristics of the probes or probes that have predetermined binding and reactivity characteristics. Regarding claim 57, Grier does not teach the step of determining the reaction or lack thereof, of each of the trapped probes with each of the targets; wherein the probes which react with the targets are segregated from the remaining probes. Regarding claim 176, Grier does not teach the segregation of probes based on binding reactivity.

With regard to claims 1, 57 and 87-88, Ulmer teaches selecting probes based on predetermined binding and reactivity characteristics of the probes and that the probes have predetermined binding and reactivity characteristics (col. 7, lines 28-35, where the trapped probe is an oligonucleotide or nucleic acid fragment)

With regard to claim 57, Ulmer teaches an embodiment comprising determining the reaction or lack thereof, of each of the trapped probes with each of the targets; wherein the probes which react with the targets are segregated from the remaining probes (col. 7, lines 16-44, where probes that are bound to the target are separated from the remaining probes).

With regard to claim 176, Ulmer teaches an embodiment of claim 57, wherein at least two of the probes have binding or reactivity characteristics that differ from one another and at least one of the probes is selected by segregating the probe based on its different binding or reactivity characteristic by moving the probe to a predetermined location within the vessel and using the location of the segregated probe to select the probe (col. 7, lines 16-44, where probes that are bound to the target are separated from the remaining probes).

Regarding claims 1 and 87-88, while Grier teaches the use of a personal computer to identify particles, Grier does not explicitly teach computerized monitoring of the positions of the optical traps. Visccher teaches an overview of the construction of multiple-beam optical traps and includes different methods of monitoring (Abstract).

With regard to claim 1, Visccher teaches tracking a position of at least one optical trap by computerized monitoring (p. 1066, col. 1; p. 1070-1073, where position detection options are discussed; p. 1071, col. 1, where the position detection is described in detail).

With regard to claims 87-88, Visccher teaches tracking a position of at least one of the trapped probes in the array by computerized monitoring of the position of the optical trap which contains it (p. 1066, col. 1; p. 1070-1073, where position detection options are discussed; p. 1071, col. 1, where the position detection is described in detail).

With regard to claim 158, Visccher teaches an embodiment of claim 57, further comprising tracking the position of at least one of the trapped probes by monitoring the position of the optical trap which contains it (p. 1066, col. 1; p. 1070-1073, where position detection options are discussed; p. 1071, col. 1, where the position detection is described in detail).

With regard to claim 160, Visccher teaches an embodiment of claim 57, further comprising producing an optical data stream of data corresponding to the identity and position of at least one of the optical traps (p. 1066, col. 1; p. 1070-1073, where position detection options are discussed; p. 1071, col. 1, where the position detection is described in detail).

With regard to claim 164, Visccher teaches an embodiment of claim 160, further comprising receiving the optical data-stream with a computer (p. 1070-1073, where position detection options are discussed and include imaging onto a photodiode after magnification by a microscope; see also p. 1074, where the position detection is carefully calibrated and includes calibration of the video system).

With regard to claim 165, Visccher teaches an embodiment of claim 164, further comprising analyzing the optical data stream with the computer (p. 1070-1073, where position detection options are discussed and include imaging onto a photodiode after magnification by a microscope and includes subsequent analysis).

With regard to claim 167-169, Visccher teaches an embodiment of claim 166, further comprising converting the optical data-stream to a video signal, receiving the video signal and analyzing the video signal with a computer (p. 1070-1073, where position detection options are discussed and include imaging onto a photodiode after magnification by a microscope; see also p. 1074, where the position detection is carefully calibrated and includes calibration of the video system).

With regard to claim 171, Visccher teaches an embodiment of claim 170, wherein the video signal is used to produce an image (p. 1070-1073, where position detection options are discussed and include imaging onto a photodiode after magnification by a microscope; see also



p. 1074, where the position detection is carefully calibrated and includes calibration of the video system; Figure 7, where an image is produced).

With regard to claim 172, Visscher teaches an embodiment of claim 171, further comprising viewing the image and directing the movement of one or more of the optical traps based on the viewing of the image (p. 1070-1073, where position detection options are discussed and include imaging onto a photodiode after magnification by a microscope; see also p. 1074, where the position detection is carefully calibrated and includes calibration of the video system; Figure 7, where an image is produced).

With regard to claim 173, Visscher teaches an embodiment of claim 160, wherein the data is spectroscopic data (p. 1070-1073, where position detection options are discussed and include a variety of position detection data types).

With regard to claim 174, Visscher teaches an embodiment of claim 173, further comprising using a computer to direct the movement of one or more optical traps based on an analysis of the spectroscopic data (p. 1070-1073, where position detection options are discussed; see also p. 1074, where the position detection is carefully calibrated).

With regard to claim 190, Visscher teaches an embodiment of claim 57, wherein the movement of at least one optical trap is selected from one or more of the group consisting of rotation in a fixed position, rotation in a non- fixed position, movement in two dimension, and movement in three dimensions (p. 1070-1076, where a variety of types of movement are detected in different dimensions, depending on the format of position detection chosen).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the probe with predetermined binding and reactivity

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characteristics as taught by Ulmer into the method of optical trapping taught by Grier to arrive at the claimed invention with a reasonable expectation for success. Ulmer discloses the use of optical traps in methods of biological, biochemical or chemical processes. As taught by Ulmer, “Examples of chemical, biochemical and/or biological processes that might be implemented in accordance with the invention include the following: oligonucleotide synthesis and sequencing, carbohydrate synthesis and sequencing, combinatorial library synthesis and screening, conventional (i.e., Sanger or Maxam-Gilbert) DNA sequencing, or single-molecule DNA sequencing” (Abstract). Specifically regarding binding and reactivity characteristics of the probes, Ulmer teaches, “procedures which permit the identification and isolation of the desired DNA fragment from among the background of undesired DNA fragments. The optical trap described herein may be used to simplify or obviate these latter procedures”. Ulmer also teaches, “a probe (a nucleic acid fragment that specifically binds to the desired nucleic acid fragment) is necessary. The probe is coupled to a particle suitable for trapping in the optical trap. One or more of the particle-coupled probes are then applied to thin film 110 in a first droplet 112. The optical trap is then used to select one of the particle-coupled probes in its optical beam and move the particle-coupled probe through thin film 110 (col. 7, lines 28-35).” In fact, it is also a directly stated object of Grier to “provide an improved method and system for establishing a plurality of optical traps for a variety of commercial applications relating to manipulation of small particles” and this includes chemical and biochemical sensor arrays, facilitation of combinatorial chemistry applications and the manipulation of biological materials (col. 1, lines 48-57). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to extend the arrays of optical traps taught by Grier to include the specific types

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of biological targets and probes with predetermined or predefined binding and reactivity characteristics as taught by Ulmer to achieve the manipulation of biological targets as described generally by Grier with a reasonable expectation for success.

Furthermore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Grier and Ulmer to incorporate the computerized monitoring of Visscher to arrive at the claimed invention with a reasonable expectation for success. As taught by Visscher, “sensitive position detectors for objects trapped by the system are required. A wide temporal bandwidth is desirable for such detectors (>10 kHz), especially for calibration of optical trap stiffness)” (p. 1066, col. 1). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Grier and Ulmer to incorporate the computerized monitoring of Visscher to arrive at the claimed invention with a reasonable expectation for success.

### ***Response to Arguments***

5. Applicant's arguments with respect to claims 1, 13, 18, 57, 61, 87-88, 112, and 158-206 have been considered but are moot in view of the new ground(s) of rejection. The arguments are focused on the claims as amended, which required the new grounds of rejection.

### ***Conclusion***

No claims are allowed. All claims stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephanie K. Mummert/  
Patent Examiner, Art Unit 1637

SKM  
July 5, 2008